

AMENDMENTS TO THE SPECIFICATION:

Please replace the paragraph on page 6, lines 15-18, with the following paragraph:

In one embodiment of the invention, the recombinant tissue protective cytokine comprises one or more altered amino acid residue between position 11 to 15 of SEQ ID NO:10 [SEQ ID NO:1], position 44 to 51 of SEQ ID NO:10 [SEQ ID NO:2], position 100-108 of SEQ ID NO:10 [SEQ ID NO:3], or position 146-151 of SEQ ID NO:10 [SEQ ID NO:4].

Please replace the paragraph on page 15, lines 4-8, with the following paragraph:

In one embodiment, at least one tyrosine residue of a recombinant tissue protective cytokine may be modified in an aromatic ring position by an electrophilic reagent, such as by nitration or iodination. In a related embodiment, the recombinant tissue protective cytokine as described herein above comprises at least one lysine residue modified by 2,4,6-trinitrobenzenesulfonate trinitrobenzenesulfonate sodium or another salt thereof.

Please replace the paragraph on page 19, lines 20-26, with the following paragraph:

According to one aspect of the invention, there is provided a method for protecting, maintaining or enhancing the viability of a cell, tissue, or organ isolated from a mammalian body comprising exposing said cell, tissue, or organ to a pharmaceutical composition comprising a recombinant tissue protective cytokine comprised of an erythropoietin that lacks at least one erythropoietic activity selected from the group consisting of increasing hematocrit, vasoactive action (vasoconstriction/vasodilatation), hyperactivating platelets, pro-coagulant activity and increasing production of thrombocytes. In certain embodiments, the protection does not affect bone marrow.

Please replace the paragraph on page 21, lines 24-33, with the following paragraph:

The invention also provides for the use of a molecule in association with a recombinant tissue protective cytokine as described herein above, lacking at least one erythropoietic activity selected from the group consisting of increasing hematocrit, vasoactive action (vasoconstriction/vasodilatation), hyperactivating platelets, pro-coagulant activities, and increasing production of thrombocytes, for the preparation of a pharmaceutical composition for transporting a molecule via transcytosis across an endothelial cell barrier. In one embodiment, the association is a labile covalent bond, a stable covalent bond, or a non-covalent association with a binding site for said molecule. In another embodiment, the molecule is a receptor agonist or antagonist hormone, a neurotrophic factor, an antimicrobial agent, a

radiopharmaceutical, an antisense oligonucleotide, an antibody, an immunosuppressant, a dye, or a marker, or an anti-cancer drug.

Please replace the paragraph on page 48, line 13, with the following paragraph:

S146A, N147K, N147A, F148Y, ~~P148A~~ F148A, L149A, R150A, R150E, G151A,

Please replace the paragraph on page 48, line 18, with the following paragraph:

~~C160S~~ A160S, C161A, or R162A.

Please replace the paragraph on page 49, line 18, with the following paragraph:

Certain modifications or combinations of modifications can effect the flexibility of a erythropoietin muteins effecting binding to a receptor, such as the erythropoietin receptor or a secondary receptor to which erythropoietin or an erythropoietin mutein binds. Examples of such modifications or combinations thereof useful in the compositions and methods of the invention, include, but are not limited to, K152W, R14A/Y15A, I6A, C7A, D43A, P42A, F48A, Y49A, T132A, I133A, T134A, N147A, ~~P148A~~ F148A, R150A, G151A, G158A, C161A, and R162A. Corresponding mutations are known to be detrimental in human growth hormone (Wells et al.). In certain embodiments, the recombinant tissue protective cytokine mutein of the invention does not comprise one or more of the above substitutions. In certain embodiments the pharmaceutical compositions of the invention comprising the recombinant tissue protective cytokine mutein of the invention do not comprise one or more of the above substitutions. In certain embodiments the use and treatment methods of the invention which utilize the recombinant tissue protective cytokine mutein of the invention do not comprise one or more of the above substitutions.

Please add the following paragraph at page 90, after line 10:

All amino acid positions in the erythropoietin sequences and mutants recited herein, unless prefixed with the term “full length,” refer to their positions in the mature protein. For example, the erythropoietin region TKVNFYAW (SEQ ID NO:2) is designated herein as amino acids 44-51 of native, human erythropoietin. In the sequence listing for SEQ ID NO:10, TKVNFYAW is present at positions 71 to 78, owing to the presence of the 27-amino acid leader sequence. That is, position 1 in the mature protein corresponds to position 28 in the sequences listed in the full length sequence above and in the sequences (SEQ ID NOs:10, 15-119) provided in the accompanying sequence listing.

Please replace the paragraph on page 118, lines 17-18, with the following paragraph:

6.13. EXAMPLE 13: ANTI-INFLAMMATORY EFFECTS~~AFFECTS~~ OF ERYTHROPOIETIN

Please replace the paragraph on page 122, lines 22-23, with the following paragraph:

6.14. EXAMPLE 14: NMDA INDUCED ~~CALL~~CELL DEATH ASSAY